

## **I. Amendments to the Claims:**

This listing of claims shall replace all prior versions, and listings, of the claims in the application.

## **II. AMENDMENTS TO THE SPECIFICATION**

At the paragraph on page 7, lines 9-16, please amend as follows:

--One major disadvantage to the current use of buprenorphine in detoxification program is its low and inconsistent oral absorption, making it impractical for daily oral dosing. There are sublingual tablets and transdermal dosage forms, but in countries where these have been marketed, there have been cases of abuse with addicts preparing them for injection. An ~~indietable~~ injectable controlled release delivery system would (1) avoid oral absorption problems, (2) circumvent the abuse problems associated with sublingual and parenteral forms and (3) addresses one of the major obstacles in agonist therapy – patient compliance.--

Please insert the following new paragraphs following page 11, line 11 of the original specification which corresponds to following paragraph [0029] on page 3, column 2 of the corresponding United States Publication No. US 2005/0048115A1.

--[0029.1] In certain embodiments, the invention is directed to a pharmaceutical formulation for extended release of buprenorphine from microspheres, said formulation made by steps comprising: admixing PLGA having a first specific viscosity with PLGA having a second specific viscosity to form a PLGA mixture; admixing the PLGA mixture with a halogenated organic solvent to form a PLGA-halogenated organic solvent mixture; admixing the PLGA-halogenated organic solvent mixture with buprenorphine to form a buprenorphine-PLGA-halogenated organic solvent mixture; admixing a buffered aqueous solution of PVA with the buprenorphine-PLGA-halogenated organic solvent mixture to

form an emulsion comprising microspheres, said microspheres comprising buprenorphine; recovering at least one of said microspheres from the emulsion.

[0029.2] In certain embodiments, the invention is further directed a pharmaceutical formulation where the buprenorphine with which the PLGA-halogenated organic solvent mixture is admixed comprises buprenorphine free base. In certain other embodiments, the buprenorphine with which the PLGA-halogenated organic solvent mixture is admixed consists essentially of buprenorphine free base.

[0029.3] In certain embodiments, the invention is further directed to a pharmaceutical formulation wherein the buffered aqueous solution of PVA comprises phosphate.

[0029.4] In certain other embodiments, the invention is also directed to a pharmaceutical formulation wherein the concentration of PVA in the buffered aqueous solution of PVA is about 0.1% (w/v). In certain other embodiments, the pH of the buffered aqueous solution of PVA is between about 6.8 and about 8.0. In other embodiments, the pH of the buffered aqueous solution of PVA is about 7.4.

[0029.5] In certain embodiments, the invention is directed to a pharmaceutical formulation wherein the buffered aqueous solution of PVA comprises at least one of the group consisting of sodium phosphate and potassium phosphate.

[0029.6] In certain embodiments, the invention is directed to a pharmaceutical formulation wherein the first specific viscosity is between about 0.01 and about 0.31 dL/g and the second specific viscosity is between about 0.40 and 0.88 dL/g.

[0029.7] In certain other embodiments, the invention is directed to a pharmaceutical formulation wherein the first specific viscosity is between about 0.12 and about 0.20 dL/g and the second specific viscosity is between about 0.48 and 0.80 dL/g.

[0029.8] In certain other embodiments, the invention is directed to a pharmaceutical formulation wherein the first specific viscosity is between about 0.14 and about 0.18 dL/g and the second specific viscosity is between about 0.56 and 0.72 dL/g.

[0029.9] In certain other embodiments, the invention is directed to a pharmaceutical formulation, wherein the first specific viscosity is about 0.16 dL/g and the second specific viscosity is about 0.64 dL/g.

[0029.10] In certain other embodiments, the invention is directed to a pharmaceutical formulation wherein the halogenated organic solvent comprises dichloromethane.

[0029.11] In certain other embodiments, the invention is directed to a pharmaceutical formulation wherein the halogenated organic solvent consists essentially of dichloromethane.

[0029.12] In certain other embodiments, the invention is directed to a pharmaceutical formulation wherein the admixing of the buffered aqueous solution of PVA with the buprenorphine-PLGA-halogenated organic solvent mixture comprises sonication.

[0029.13] In certain other embodiments, the invention is directed to a formulation wherein the recovering comprises at least one of the group consisting of sedimentation and lyophilization.

[0029.14] In certain other embodiments, the invention is directed to a process for making a pharmaceutical formulation for extended release of buprenorphine from microspheres, said process comprising: admixing PLGA having a first specific viscosity with PLGA having a second specific viscosity to form a PLGA mixture; admixing the PLGA mixture with a halogenated organic solvent to form a PLGA-halogenated organic solvent mixture; admixing the PLGA-halogenated organic solvent mixture with buprenorphine to form a buprenorphine-PLGA-halogenated organic solvent mixture; admixing a buffered aqueous solution of PVA with the buprenorphine-PLGA-halogenated organic solvent mixture to

form an emulsion comprising microspheres, said microspheres comprising buprenorphine; recovering at least one of said microspheres from the emulsion.

[0029.15] In certain other embodiments, the invention is directed to a process wherein the buffered aqueous solution of PVA comprises at least one of the group consisting of sodium phosphate and potassium phosphate.

[0029.16] In certain other embodiments, the invention is directed to a process wherein the buprenorphine consists essentially of buprenorphine free base.

[0029.17] In certain other embodiments, the invention is directed to a method of treating a mammal in which treatment with buprenorphine is indicated, said method comprising the step of administering to the mammal a pharmaceutically effective quantity of buprenorphine-containing microspheres prepared by a process comprising: admixing PLGA having a first specific viscosity with PLGA having a second specific viscosity to form a PLGA mixture; admixing the PLGA mixture with a halogenated organic solvent to form a PLGA-halogenated organic solvent mixture; admixing the PLGA-halogenated organic solvent mixture with buprenorphine to form a buprenorphine-PLGA-halogenated organic solvent mixture; admixing a buffered aqueous solution of PVA with the buprenorphine-PLGA-halogenated organic solvent mixture to form an emulsion comprising microspheres, said microspheres comprising buprenorphine; recovering at least one of said microspheres from the emulsion.--